US007279327B2

(12) **United States Patent**
Curtis et al.

(10) **Patent No.: US 7,279,327 B2**
(45) **Date of Patent: Oct. 9, 2007**

(54) **METHODS FOR PRODUCING RECOMBINANT CORONAVIRUS**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 33 days.

(21) Appl. No.: **10/474,962**

(22) PCT Filed: **Apr. 19, 2002**

(86) PCT No.: **PCT/US02/12453**

§ 371 (c)(1),
(2), (4) Date: **May 25, 2004**

(87) PCT Pub. No.: **WO02/086068**

PCT Pub. Date: **Oct. 31, 2002**

(65) **Prior Publication Data**

US 2004/0235132 A1 Nov. 25, 2004

Related U.S. Application Data

(60) Provisional application No. 60/285,320, filed on Apr. 20, 2001, provisional application No. 60/285,318, filed on Apr. 20, 2001.

(51) **Int. Cl.**
C12N 15/85 (2006.01)
C12N 15/63 (2006.01)

(52) **U.S. Cl.** **435/325**; 435/320.1; 424/221.1

(58) **Field of Classification Search** 435/320.1, 435/325

See application file for complete search history.

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(57) **ABSTRACT**

A helper cell for producing an infectious, replication defective, *coronavirus* (or more generally nidovirus) particle cell comprises (a) a nidovirus permissive cell; (b) a nidovirus replicon RNA comprising the nidovirus packaging signal and a heterologous RNA sequence, wherein the replicon RNA further lacks a sequence encoding at least one nidovirus structural protein; and (c) at least one separate helper RNA encoding the at least one structural protein absent from the replicon RNA, the helper RNA(s) lacking the nidovirus packaging signal. The combined expression of the replicon RNA and the helper RNA in the nidovirus permissive cell produces an assembled nidovirus particle which comprises the heterologous RNA sequence, is able to infect a cell, and is unable to complete viral replication in the absence of the helper RNA due to the absence of the structural protein coding sequence in the packaged replicon. Compositions for use in making such helper cells, along with viral particles produced from such cells, compositions of such viral particles, and methods of making and using such viral particles, are also disclosed.

14 Claims, 11 Drawing Sheets